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Dienone-phenol rearrangement of 4,4-disubstituted cyclohexadienones to multiple substituted phenols is achieved by employing Re_2O_7 as catalyst.

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Re₂O₇ Catalyzed Dienone-Phenol Rearrangement[†]

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Dienone-phenol rearrangement of 4,4-disubstituted cyclohexadienones catalyzed by Re₂O₇ was described. Multiple substituted phenols could be efficiently obtained in good to excellent yields by employing this catalytic protocol.

Although various Rhenium complexes have been synthesized and even some of them are commercially available,[1] their catalytic abilities for organic transformations are less explored compared with other transition state metal complexes.[2] In recent years, increasing interests have been dedicated to Rhenium catalysts for their stability to air and moisture, unique Lewis acidity for activation unsaturated hydrocarbon bonds.[3, 4, 5] Especially, the ability of activating C(Sp²)-H and C(Sp³)-H bonds by rhenium carbonyl complexes has enabled them to be amenable for C-H bond functionalization reactions.[2b, 3] Not only those low-valent Rhenium complexes, but also Re(V)[4] and Re(VII)[2b, 5] complexes are competent catalysts in a variety of organic transformations. For example, Toste and co-workers unveiled that Re(V)-oxo complexes enable converting propargyl alcohols to functionalized intermediates via C-C,[4b, 4c] C-O,[4e] C-N[4g] bonds formations. MeReO₃, a Re(VII) complex, is well known for its wide usage in oxidation catalyst.[5d] Besides its oxidation ability, Re(VII) also exhibit moderate Lewis acidity, which could be utilized for generation of carbocation intermediate under mild reaction conditions. For example, Re₂O₇ and PhSiOReO₃ are popular in stereospecific isomerization of allyl alcohols (Figure 1, eq. 1).[5e-5h] Those Re(VII) complexes are also used for generation of oxonium ions in acetalization and Prins reaction (Figure 1, eq. 2).[5i-5l] It's should be pointed out that the high efficiency of those reactions relies on the unique Lewis acid property of Re(VII), which could in turn stabilize the cation intermediate.
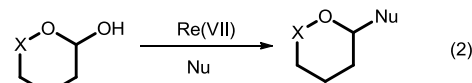
Dienone-phenol rearrangement is a rearomatization reaction of 4,4-disubstituted cyclohexadienones through bond shift, which provides a facile access to multi-substituted phenols.[6] The mechanism of Dienone-phenol rearrangement has been extensively studied and well employed in organic synthesis.[7] Typically, the reaction could be promoted by acid, strong base or photo irradiation [6] In this context, catalytic dienone-phenol rearrangement are also well described.[8] For example, Kim developed a domino dienone-phenol rearrangement/*5-endo-dig* cyclization of quinols catalyzed by PtCl₂ to afford benzofurans.[8c] Fujioka also found that transformation of dienones to benzenethioethers was efficiently achieved by catalytic TfOH.[8d] More recently, dienone-phenol rearrangement of spiro[4.5]cyclohexadienones catalyzed by Sc(OTf)₃ was described by Hamada and co-workers.[8e] In this report, we disclose that Re₂O₇ is a robust catalyst for dienone-phenol rearrangement of 4-alkoxy-substituted cyclohexadienones, which is difficult to be furnished by previous catalysts (Figure 1, eq. 3).
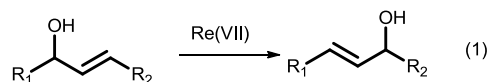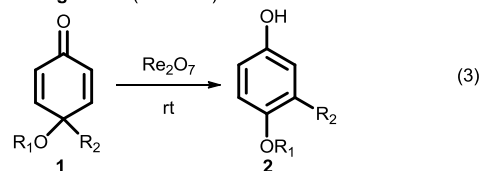

Figure 1. Representative Re(VII) catalyzed reactions involving cationic intermediate.

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As our interest in application of dienone-phenol rearrangement in synthesis of phenol **2aa**, we found that under the effect of excessive amount of BF₃•OEt, cyclohexadienone **1aa** smoothly converted to phenol **2aa** in 73% yield (Table 1, entry 1). In meanwhile, only low yield was resulted when catalytic amount of BF₃•OEt was employed (20%, Table 1, entry 2), which prompted us to investigate reaction conditions to find out a catalytic protocol for this reaction. As summarized in Table 1, most of the evaluated Lewis acids (e.g. Zn(OTf)₂, Cu(TFA)₂, AlCl₃, entry 3-9) were ineffective for this reaction with starting material being fully recovered after 12h. Previously reported catalysts such as Sc(OTf)₃[8e] and PtCl₂[8c], which served as efficient catalysts for dienone-phenol rearrangement, were also capable of facilitating the rearrangement of **1aa** albeit in 45% and 55% yield respectively (Table 1, entry 10-11). Other type promoters (e.g. TMSOTf and TfOH[8d]) gave unsatisfactory results (Table 1, entry 13-14). To our delight, Re₂O₇ worked very well for this rearrangement, providing phenol **2aa** in 92% yield with accelerating reaction rate and other Re(VII) complexes (e.g. Phe₃SiOReO₃, MeReO₃) alleviated this reaction (Table 1, entry 14-16). Subsequently, solvent screening showed that highest yield was observed in CH₂Cl₂ than using any other solvents (Table 1, entry 17-19). Low or higher temperature was detrimental to the reaction (Table 1, entry 20 and 21). Significantly, catalyst loading could be reduced to 5 mol% without deleterious effects on the reaction (Table 1, entry 22).

Table 1 Screening of reaction conditions for dienone-phenol rearrangement of quinol **1a**.[a]

1aa → conditions → **2aa**
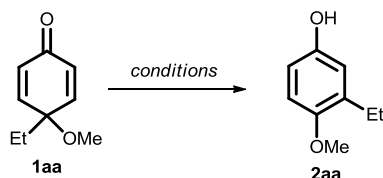
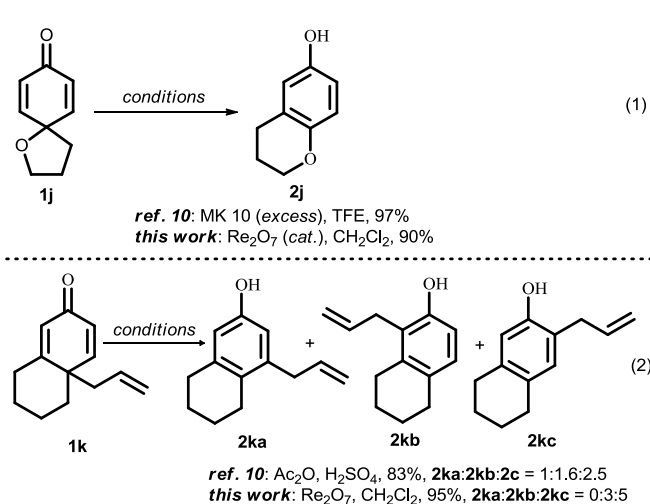| Entry	Catalyst (equiv)	T (°C)	solvent	Time (h)	Yield[b] (%)
1	BF₃•Et₂O (3.0)	rt	CH₂Cl₂	4	73
2	BF₃•Et₂O (0.1)	rt	CH₂Cl₂	4	20
3	Cu(TFA)₂ (0.1)	rt	CH₂Cl₂	12	ND
4	Zn(OTf)₂ (0.1)	rt	CH₂Cl₂	12	ND
5	Cp₂TiCl₂ (0.1)	rt	CH₂Cl₂	12	ND
6	Yb(OTf)₃ (0.1)	rt	CH₂Cl₂	12	ND
7	InCl₃ (0.1)	rt	CH₂Cl₂	12	ND
8	AgBF₄ (0.1)	rt	CH₂Cl₂	12	ND
9	AlCl₃ (0.1)	rt	CH₂Cl₂	12	ND
10	Sc(OTf)₃ (0.1)	rt	CH₂Cl₂	12	45
11	PtCl₂ (0.1)	rt	CH₂Cl₂	4	55
12	TMSOTf (0.1)	rt	CH₂Cl₂	4	60
13	HOTf (0.1)	rt	CH₂Cl₂	4	50
14	Re₂O₇ (0.1)	rt	CH₂Cl₂	1	92
15	Ph₃SiOReO₃ (0.1)	rt	CH₂Cl₂	1	83
16	MTO (0.1)	rt	CH₂Cl₂	12	ND
17	Re₂O₇ (0.1)	rt	toluene	12	22
18	Re₂O₇ (0.1)	rt	CHCl₃	12	67
19	Re₂O₇ (0.1)	rt	EtOAc	12	16
20	Re₂O₇ (0.1)	0	CH₂Cl₂	12	50
21	Re₂O₇ (0.1)	40	CH₂Cl₂	1	76
22	Re₂O₇ (0.05)	rt	CH₂Cl₂	1	93

[a] Reaction conditions: quinol **1aa** (0.1 mmol) in CH₂Cl₂ (0.5 mL) was added dropwise to a solution of catalyst (0.01 mmol) in CH₂Cl₂ (0.5 mL) at rt. [b] Isolated yields.

Upon identification of reaction conditions, the substrate scope of the reaction was subsequently examined. Various cyclohexadienones were prepared by phenol oxidation and subjected to the standard reaction conditions (Scheme 1). Satisfactorily, different alkoxy groups were compatible, affording corresponding phenols in good to excellent yields (**2aa** to **2ag**). Different protecting groups were also surveyed for exploring functional groups compatibility of this reaction. Given the fact that Brønsted acids were usually generated from hydrolysis of Re₂O₇,[5] acid-labile protecting groups (e.g. TBS, Boc for **2ba** and **2bb**) were not well tolerated, leading to low isolated yields due to substantial deprotection.[9] Moderate yields could be obtained when acid-stable protecting groups were presented (e.g. Ac, Bz, Ts for **2bd**-**2bf**). Next, different migration groups were evaluated for this reaction. Cyclohexadienones with primary and secondary alkyl groups smoothly transferred to corresponding phenols in very high yields (**2ca** to **2ci**). However, cyclohexadienone **1d** with 4-methyl was inert under reaction conditions, owing to the low migratory aptitude of methyl and moderate Lewis acidity of Re₂O₇. Tertiary butyl was also an unsuitable migratory group and 4-methoxypheol was exclusively formed from **1e**, presumably via extrusion of stable tertiary carbocation (see Supporting Information). Disappointingly, only sluggish reaction mixture was obtained when cyclohexadienone **1f** was examined. Furthermore, tetra-substituted phenols could be isolated regioselectively from multiple substituted cyclohexadienone in good yields, with migratory group being attached to less hindered position (**2g** to **2i**). Additionally, the reaction could also be easily scaled up without influencing the isolated yields (**2g** and **2h**).
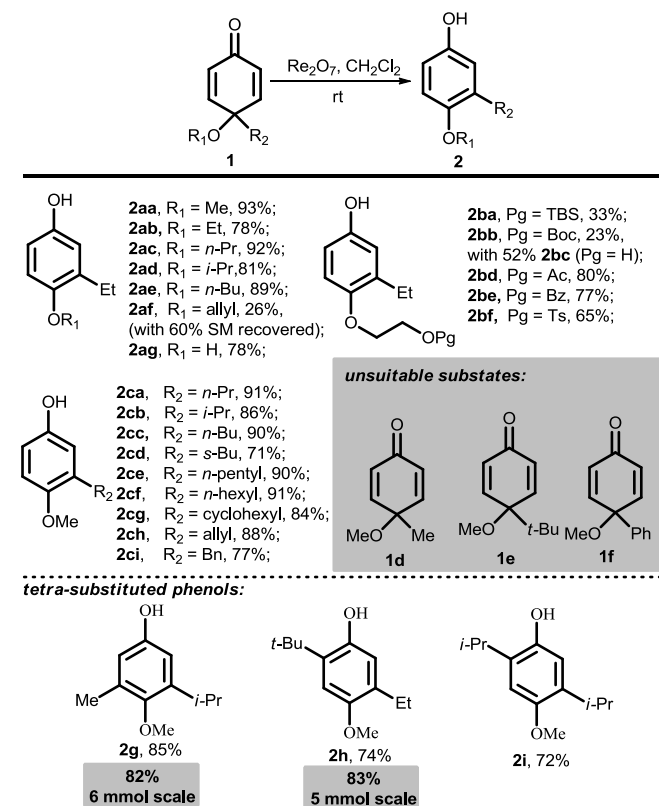
Scheme 1 Substrate scope of the Re$_2$O$_7$ catalyzed dienone-phenol rearrangement.

Scheme 2 Other substrates.

To demonstrate the efficiency of Re$_2$O$_7$ on dienone-phenol rearrangement, a direct comparison with previous protocols was made by using cyclohexadienones **1j** and **1k** as substrates (Scheme 2). In Kita's report,[10] spiro-cyclohexadienone **1j** could be transferred to chroman **2j** quantitatively, promoted by excess amount of montmorillonite K10 (Scheme 2, eq. 1). Pleasingly, under the effect of catalytic Re$_2$O$_7$, chroman **2j** could be furnished in comparable yield. Furthermore, rearrangement of cyclohexadienone **1k** led to three regioisomers **2ka**, **2kb** and **2kc** in 1:2.5:1.6 ratios under the effect of Ac$_2$O/H$_2$SO$_4$ as a result of competitive [1,2]-shift and [3,3]-rearrangement of allyl (Scheme 2, eq. 2).[11] In sharp contrast, under our reaction conditions only [3,3]-shift product **2kb** and **2kc**[11] was obtained in 95% combined yield and 3:5 ratio, showing that reaction pathways was greatly influenced by using Re$_2$O$_7$ as catalyst.

Conclusions

Re$_2$O$_7$ catalyzed dienone-phenol rearrangement reaction is developed. Multiple substituted phenols could be conveniently prepared in good to excellent yields by using this catalytic procedure. In addition, [3,3]-shift product is exclusively formed under the effect of Re$_2$O$_7$ when the migratory group is allyl. The highly catalytic efficiency of Re$_2$O$_7$ on dienone-phenol rearrangement is attributed to the moderate Lewis acidity of Re$_2$O$_7$ and its ability of stabilizing putative phenyl cation intermediate of this reaction.

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† Electronic Supplementary Information (ESI) available: General experimental procedures and spectroscopic date for the all compounds. For ESI or other electronic format See DOI: 10.1039/c000000x/

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